

Differences in the Effect of Giving Fe Tablets and Capsules Moringa Leaves on Hepcidin and Ferritin Levels in Anemic Pregnancy Rats

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Abstract

Anemia is a condition characterized by a decrease in Hemoglobin (HB), a serious global public health problem especially affecting children and pregnant women. This study aimed to determine differences in the effect of giving Fe tablets and capsules of Moringa leaves on hepcidin and ferritin levels in anaemic pregnancy rats. This research was an experimental study with a randomized post-test-only control group design. This research was conducted at the Animal House of the Faculty of Medicine, Andalas University to maintain and treat experimental animals. Ferritin and Hepcidin examinations were carried out at the biomedical laboratory of the Faculty of Medicine, Andalas University. The sample in this study were female white rats (Rattus Novergicus) which met the inclusion and exclusion criteria, the data were analyzed using One Way Anova. The results of this study indicated that the mean hepcidin levels in the Fe (P1) and Moringa leaf capsule (P2) groups were 181.902 ± 20.31 and 216.362 ± 29.90 with a p-value of 0.006 . The mean ferritin levels in the Fe(P1) and Moringa leaf capsule (P2) groups were 1.928 ± 0.263 and 2.308 ± 0.320 with a p-value of 0.004. The conclusion in this study was that there was an effect on hepcidin levels after being given Fe tablets (P1) and Moringa leaf capsules (P2) to anemic pregnant rats and there was an effect on ferritin levels after being given Fe tablets (P1) and Moringa leaf capsules (P2) to anemic pregnant rats

Keywords : Anemic, Ferritin, Fe Tablets, Hepcidin, Moringa Leaf Capsules

INTRODUCTION

Anemia is a condition or condition characterized by a decrease in haemoglobin (Hb) levels, hematocrit or red blood cell count. Hb and blood cell levels vary greatly depending on age, gender, altitude, and certain physiological conditions (Turawa et al., 2021). Anemia is more common in pregnancy because the need for nutrients increases and changes occur in the blood and bone marrow (Millah, 2019). Word Health Organization estimates that 40% of pregnant women worldwide and 42% of children under 5 suffer from anemia. Anemia is a serious global public health problem that primarily affects children and pregnant women (WHO, 2017).

The prevalence of anemia in pregnant women in Indonesia has increased compared to 2013, in 2013 there were 37.1% of pregnant women with anemia, while in 2018 it increased to 48.9% (Kemenkes RI, 2018). Meanwhile, according to the Central Statistics Agency, anemia in pregnant women in 2018 was 48.9% (BPS, 2019). The incidence of anemia in pregnant women in West Sumatra Province based on the Nutrition Status Monitoring Survey conducted by the West Sumatra Provincial Health Office in 2015 was 43.1%. For the City of

Padang, the coverage of anemic pregnant women is 11.2% with an absolute number of 2044 people out of 14,589 pregnant women.

Pregnant women who are anemic have a risk of death up to 3.6 times greater than pregnant women who are not anemic. Anemia also has a high contribution to death in Indonesia with a percentage reaching 50-70%. In addition, pregnant women who suffer from anemia can impact the fetus, such as babies born prematurely, the risk of low birth weight babies, fetal abnormalities, and an increased risk of fetal distress (Sumailan et al., 2021). There are many weaknesses of chemical drugs which have side effects that make consumers uncomfortable, high drug resistance, and the possibility of accumulation in the body. This causes people to choose to utilize natural local food as a substitute for chemical drugs (Pane et al., 2021).

Moringa (Moringa oleifera Lam) is a local plant known for centuries as a multi-purpose, nutrient-dense and medicinal plant containing more and various natural compounds than any other plant species. According to research results, Moringa leaves contain very high amounts of vitamin A, vitamin B, vitamin C, calcium, potassium, iron and protein which are easily digested by the human body. The high iron content (Fe) in dried Moringa leaves or in the form of Moringa leaf flour, which is equivalent to 25 times higher than spinach, can be used as an alternative for the natural prevention of anemia in pregnant women (Kurniasih, 2013).

To prevent anemia during pregnancy and maintain optimal fetal growth, proper regulators are needed to regulate iron homeostasis in the body. One iron regulator is hepcidin, a protein whose production is found in the liver (Agustina, 2019).

Iron reserves stored in ferritin also play an important role because a person's iron status can be assessed from the iron reserves in the body and ferritin is used as a reliable and sensitive parameter to determine iron reserves in healthy people. Ferritin is widely used in clinical practice and population monitoring. Serum ferritin < 12 mg/dl is highly specific for iron deficiency, meaning it is depleted of all iron stores, so it can be considered diagnostic. Low serum ferritin indicates an early onset of iron deficiency (Gumilang et al., 2021).

Hepcidin levels and ferritin levels in anemic pregnant women are closely related. To diagnose anemia in pregnant women, apart from a physical examination, laboratory tests are also needed so that the results are more accurate in distinguishing the types of anemia. Laboratory tests such as ferritin and hemoglobin levels have become routine for diagnosing iron deficiency anemia (Diana, 2017).

According to Diana (2017) about Differences in Hepcidin and Ferritin Levels Between Anemia and Non-Anemia Pregnant WomenAnemia states thathepcidin level with anemia was 8.58 ± 2.49 ng/ml and without anemia was 6.66 ± 2.76 ng/ml ($p < 0.05$), while for ferritin level with anemia was 21.86 ± 22, 37 ng/ml and not anemic was 46.48 ± 48.14 ng/ml ($p < 0.05$).This study concludes that there is a significant difference between hepcidin levels and ferritin levels with anemia and without anemia in pregnant women.

This study aimed to show differences in the effect of giving Fe tablets and capsules Moringa leaves on hepcidin and ferritin levels anemic pregnancy rats. The benefit of this study is that the management of anemia in pregnant women by administering Fe tablets and Moringa leaf capsules can reduce maternal mortality and morbidity. Hepcidin and ferritin can be used as one of the parameters for the occurrence of anemia. Based on the background that has been stated, the researchers were interested in examining the effect of giving Fe tablets and Moringa leaf capsules on ferritin and hepcidin levels in anemic pregnant rats.

METHODS

This research is an experimental research with a randomized post test only control group design. This study used a true experiment design, with the Post Test Group Design design which aims to determine differences in the effect of Fe tablets and Moringa Leaf Capsules on Hepcidin and Ferritin Levels in Anemia Pregnant Rats. This research was conducted at the Animal House of the Faculty of Medicine, Andalas University to maintain and treat experimental animals. Ferritin and Hepcidin examinations were conducted at the Biomedical Laboratory, Faculty of Medicine, Andalas University, Padang. This research was conducted from June to September 2022. The population in this study were female white rats (Rattus Novergicus). The selection of female Wistar rats was based on the consideration that rats are experimental mammals or often called laboratory animals, because they are often used in biomedical research.

The research samples were randomly selected female white rats (Rattus norvegicus), 2-3 months old and 200-250 gram body weight. The research sample is part of the population that meets the inclusion and exclusion criteria. The sample size in this study was calculated using the Federer formula (1977) so sample 30 rats. The sample in this study were 30 pregnant rats with anemia, divided into two treatment groups: the Fe tablet supplementation group and the Moringa leaf capsule supplementation group, which were determined by simple randomization.

This research was conducted after obtaining ethical clearance from the research ethics committee. The statement of passing the ethical review came from the Research Ethics Committee of the Faculty of Medicine, Andalas University, Padang with certificate No: 906/UN.16.2/KEP-FK/2022.

The flow in this study was that the rats were acclimatized for one week, and then the rats were injected intraperitoneally with $nano_2$ of 25 mg/kg for 18 days. The rat was then mated with a 3:1 ratio then the rat is pregnant, make sure the rat was pregnant by looking presence of vaginal plugs, group the rats into 3 groups, checked hemoglobin levels, hepcidin levels and ferritin levels rat, rats that had been divided into 3 groups, positive control group, treatment group I (P1) Fe tablet dose of 1.08 mg/day given on day 1 to 20 of gestation and treatment group II (P2) Moringa Leaf Capsule dose 4 capsules/day at a dose of 36 mg/200 g bw of rats for 20 days. After that, measure the Hepcidin And Ferritin levels of the rats after treatment, induction by giving $NaNO_2$ via intraperitoneal for 25 mg/kg body weight for 18 days. Provision of Fe tablets at a dose of 1.08 mg/day was given on the day to 1 to 20 gestations, Giving Moringa Leaf Capsules 4 capsules/day with a dose of 36 mg/200 gr Bw for 20 days.

Data from the research results were collected in an observation sheet as a technical guide for implementing the intervention, which included a sample code. Research data collection will be carried out by the authors and laboratory instructors related to labour guidance and direction. The animal house staff at the Faculty of Pharmacy, Andalas University supervised the data on the hemoglobin level of the rats. In contrast, the Hepcidin and Ferritin levels data were supervised by the Biomedical Labor instructor, Faculty of Medicine, Andalas University. One Way Anova parametric statistical test is performed with a degree of confidence of 95% (α=0.05).

RESULTS

The research sample was female white rats (Rattus norvegicus) who experienced anemia and were randomly selected, aged 2-3 months with a body weight of 200-250 grams which were divided into three groups, namely the control group with 10 samples each, the group given the Fe tablet intervention (P1), and the group that was given the moringa leaf capsule intervention (P2).

The mean levels of hepcidin and ferritin in pregnant anemic rats in the control group (K), treatment 1 (P1), and treatment 2 (P2) can be seen in Table 5.1 as follows:

Table 1. Average Hepcidin and Ferritin Levels of Anemia Pregnant Rats in the control group (K), treatment 1 (P1), and Treatment 2 (P2)

Variable	Sample	Before		After		Δ
		(Mean ± SD)	(Min-Max)	(Mean ± SD)	(Min-Max)	
Hepcidin (ηg/ml)	Control (K)	193.791 ± 24.84	147,241-224,925	196.674 ± 10.64	171,871-211,401	2.88
	Treatment 1 (P1)	170.341 ± 31.25	108.077-215.677	181.902 ± 20.31	133.222-199.605	11.56
	Treatment 2 (P2)	189.515 ± 18.60	163,697-230,570	216.362 ± 29.90	179,701-275,104	26,84
Ferritin (ηg/ml)	Control (K)	2.168 ± 0.224	1.866-2.472	1.940 ± 0.189	1.674-2.330	-0.22
	Treatment 1 (P1)	2.067 ± 0.274	1.622-2.522	1.928 ± 0.263	1.518-2.300	-0.13
	Treatment 2 (P2)	2.176 ± 0.228	1.902-2.589	2.308 ± 0.320	1.869-2.805	0.13

Based on Table 1, the average hepcidin level in the Moringa leaf group (P2) was higher than the other two groups, with a difference in levels after administration of 26.84 ηg/ml. The average ferritin level in the Moringa leaf group (P2) was higher than the other two groups, with a difference in levels after administration of 0.13 ηg/ml. Before the One-way Anova test was carried out, the overall data normality test was carried out using the Shapiro-Wilk test and the following results were obtained:

Table 2. Data Normality Test

Examination Rate	Sample	*p-values*
Hepcidin Before	Control	0.289
	Fe tablets	0.648
	Moringa Leaf Capsules	0.450
Hepcidin After	Control	0.171
	Fe tablets	0.127
	Moringa Leaf Capsules	0.549
Ferritin Before	Control	0.302
	Fe tablets	0.992
	Moringa Leaf Capsules	0.189
Ferritin After	Control	0.621
	Fe tablets	0.671
	Moringa Leaf Capsules	0.575

Based on the data normality test results in Table 2, all variables are normally distributed (p value > 0.05) and can be continued using the One Way Anova test.

Table 3. Analysis of the Effect of Fe Tablets and Moringa Leaf Capsules on Hepcidin Levels of Pregnant White Rats (Rattus Norvegicus) Control Group and Treatment Group

Group	N	Hepcidin Levels (μg/ml) Mean ± SD	*p-values*
K	10	196.67 ± 10.64	
P1	10	181.90 ± 20.31	0.006
P2	10	216.36 ± 29.90	

Information :

*p ≤ 0.05 with One Way Annova

K+ : The group of pregnant rats without treatment

P1 : The pregnant rat group was given Fe tablets

P2 : The pregnant rat group was given Moringa Leaf Capsules

Based on table 3, it was found that the average hepcidin level in the Moringa leaf group (P2) was higher than the other two groups, namely 216.36 ± 29.90. Statistically, Fe tablets and Moringa leaf capsules had an effect on Hepcidin levels (p<0.006).

To see the differences in each group, a Post Hoc test was carried out with the following results:

Table 4. LSD Post Hoc Test Results for the Effect of Fe Tablets and Moringa Leaf Capsules on Hepcidin Levels in Pregnant White Rats (Rattus Norvegicus) Control and Treatment Groups

Group	K	P1	P2
K	**-**	0.141	**0.053**
P1	0.141	-	**0.001**
P2	**0.053**	**0.001**	**-**

Information :

*p ≤ 0.05 with One Way Annova

K+ : The group of pregnant rats without treatment

P1 : The pregnant rat group was given Fe tablets

P2 : The pregnant rat group was given Moringa Leaf Capsules

The test results showed that there was a significant difference in the administration of Fe Tablets and Moringa Leaf Capsules to the hepcidin levels of white rats (Rattus novergicus) between groups P1 and P2 (p value = 0.001), and groups P2 and P1 (p value = 0.001)**.** Table 3 shows a significant difference (p<0.05) between the Fe tablet treatment group and the Moringa leaf capsule group.

Table 5. Analysis of the Effect of Fe Tablets and Moringa Leaf Capsules on Ferritin Levels in Pregnant White Rats (Rattus Norvegicus) in the Control Group and the Treatment Group

Group	N	Ferritin levels (μg/ml) Mean ± SD	*p-values*
K	10	1.94 ± 0.189	
P1	10	1.92 ± 0.26	0.004
P2	10	2.30 ± 0.32	

Information :

*p ≤ 0.05 with One Way Annova

K+ : The group of pregnant rats without treatment

P1 : The pregnant rat group was given Fe tablets

P2 : The pregnant rat group was given Moringa Leaf Capsules

Based on table 5, the average Ferritin level in the Moringa leaf group (P2) was higher than the other two groups, namely 230 ± 0.32. Statistically, Fe tablets and Moringa Leaf Capsules had an effect on Ferritin levels with a p value ($p<0.004$).

To see the differences in each group, a Post Hoc test was carried out with the following results:

Table 6. LSD Post Hoc Test Results for the Effect of Fe Tablets and Moringa Leaf Capsules on Ferritin Levels in Pregnant White Rats (Rattus Norvegicus) Control and Treatment Groups

Group	K	P1	P2
K	-	0.917	**0.004**
P1	0.917	-	**0.003**
P2	**0.004**	**0.003**	**-**

Information :

*$p \leq 0.05$ with One Way Annova

K+ : The group of pregnant rats without treatment

P1 : The pregnant rat group was given Fe tablets

P2 : The pregnant rat group was given Moringa Leaf Capsules

The test results showed that there was a significant difference in the administration of Fe Tablets and Moringa Leaf Capsules to the Ferritin levels of white rats (*Rattus novergicus*) between group K and P2 (p value= 0.004), group P1 and P2 (p-value 0.003), group P2 and control (p-value 0.004) and group P2 and P1 (p value= 0.003). Table 6 shows a significant difference ($p <0.05$) between the control group, the Fe tablet treatment and the Moringa Leaf Capsules group.

DISCUSSION

Iron is an essential micronutrient for erythropoiesis, oxidative metabolism and cellular immune response (Kurniati, 2020). Iron is only needed by the body in small amounts. Therefore, a good regulatory mechanism is needed to regulate iron absorption, distribution and secretion to maintain iron homeostasis (Krisnanda, 2020). Iron deficiency will cause disorders of hematopoiesis and cellular metabolism, while excess iron can result in cell death due to the formation of free radicals (Wahyuni, 2021).

One of the substances that play a role in maintaining iron levels in the body is hepcidin and ferritin. Apart from being a regulator of iron levels in the blood, hepcidin is also known to

act as a mediator of anemia in chronic disease, while ferritin functions as the main protein for iron storage which describes the reserves of iron stored in the body (Mani et al., 2020).

In theory, iron absorption in the intestine consists of 3 phases, namely the luminal phase, the mucosal phase, and the systemic or corporeal phase. Iron bonds from foodstuffs (moringa) are released or converted into dissolved and ionized forms in the luminal phase. Then the iron in the ferric form ($Fe3+$) is reduced to the ferrous form ($Fe2+$) so that it is ready to be absorbed by the intestine. In this process, gastric juice plays an important role. The best absorption occurs in the duodenum and proximal jejunum. This relates to the number of receptors on the intestinal surface and pH. In 100 grams of Moringa powder contains many amino acids, which here can help prevent the polymerization process and iron precipitation.

Besides that, In Moringa there is vitamin C (ascorbic acid) which is a very strong iron absorption booster which functions as a reducing agent that can convert ferrous into ferrous, maintains intestinal pH low to prevent iron precipitation and acts as a monomeric chelator which forms iron-ascorbate chelate which more easily absorbed by the body. After that, iron is actively absorbed through the receptors. If the dose is too large, iron will enter by passive diffusion. In the enterocyte cells, iron will be bound by a specific protein carrier and transferred through the cells to the capillaries or stored in the form of ferritin in the enterocytes and then excreted along with desquamation of the intestinal epithelium. In the systemic phase, iron that enters the plasma will be bound by apo transferrin to become transferrin and circulate throughout the body, especially to erythroblast cells in the bone marrow. All cells have transferrin receptors on their surface. Haemoglobin which functions to transport O2 throughout the cell. The availability of sufficient haemoglobin makes the metabolic system work properly.

Based on Table 1 shows that the average hepcidin level in the Moringa leaf group (P2) is higher than the other two groups. Based on Table 3 from the One-way Anova analysis test results, there is an effect on hepcidin levels after being given Fe tablets (P1) and Moringa leaf capsules (P2) in anaemic pregnant rats with a p-value = 0.006. Based on Table 4, it was found that there was a significant difference in hepcidin levels in the rat group after being given Fe tablets (P1) and Moringa leaves (P2) with a p-value = 0.001.

Iron (Fe) is one of the factors that form hemoglobin that transports O2 throughout cells. The availability of sufficient hemoglobin makes the metabolic system work well to determine iron status in the body. Iron deficiency is defined as a condition where no iron can be mobilized, resulting in long-term iron imbalance, ultimately leading to the disruption of iron to the body's tissues.

There are three stages of iron deficiency anaemia: the first stage is iron depletion, the second stage is called iron deficiency erythropoiesis and the third stage is called iron deficiency anaemia. Deficiency occurs, characterized by a decrease in serum (Young et al., 2018). Ferritin is the main iron storage protein that describes the body's reserves of iron stores (Saito, 2014).

The biochemical examination needs to be done to determine the presence of iron deficiency early before the occurrence of iron deficiency anemia. Serum ferritin is a clinical biomarker that can be used to detect iron deficiency. The normal category of serum ferritin is in the range of 18 – 270 mg/L. The World Health Organization (WHO) criteria used to define depleted iron stores or iron deficiency are less than 18 mg/L for women over 5 years old (Arima et al., 2019). Serum ferritin levels indicate the availability of body iron because protein binds to iron reserves in the body. Serum ferritin is also an acute phase reactant, so it can increase in chronic inflammation and infection.Anemia is a condition of decreased hemoglobin levels, hematocrit and size/number of erythrocytes below normal values. This decrease can be caused by blood loss that is too fast or because red blood cell production is too slow, causing a decrease in the capacity of red blood cells to transport oxygen (Gumilang et al., 2021).

Based on Table 5.1 shows that the average ferritin level in the Moringa leaf group (P2) is higher than the other two groups. This research is in line with Jayanti (2018) research found that the mean serum ferritin levels showed significant differences in both the control group and also the treatment group starting at the beginning, mid and late pregnancy (38,314 ± 6,756 ng/mL, 85,290 ± 9,040 ng/mL, respectively, 66.5861.353 ng/mL, 56.002±5.229ng/ml). Based on the study results, it was concluded that the earlier the administration of ferrous sulfate supplements can increase serum ferritin levels.

On Anaemic pregnant rats were tested using Moringa leaf capsules at a dose of 4 capsules/day at 36 mg/200 g BW for 20 days. After that, the rat serum was taken and the ferritin and hepcidin were examined. Based on the assay results, it was found that the mean levels of hepcidin and ferritin in pregnant rats given Moringa leaf capsules increased. 100 grams of Moringa powder contains many amino acids which help the polymerisation process and precipitation of iron. Apart from that, Moringa leaves also contain vitamin C. This ingredient promotes iron absorption in the Moringa leaf capsule, which functions as a reducing agent that can convert ferrous into ferrous.

Based on Table 5.3 from the results of the One-way ANOVA analysis test, there is an effect on ferritin levels after being given Fe tablets (P1) and Moringa leaf capsules (P2) in anemic pregnant rats with a p-value = 0.004. Table 5.4 shows a significant difference in ferritin levels in the control group (K) and those given Moringa leaves (P2) with a p-value = 0.004.

After that, there was a significant difference in ferritin levels in the rats given Fe tablets (P1) and those given Moringa leaves (P2) with a p-value = 0.003.

*Moringa Oleifera*or, better known as Moringa is rich in nutrients, including iron. The iron content in Moringa Oleifera is 25 times more than spinach. Moringa leaves contain vitamins A, C, B, calcium, potassium, iron, carbohydrates, fats and proteins in very high amounts, which are easily digested and assimilated by the human body. Moringa leaves are the leaves of the Moringa tree, which contain various macro and micronutrients, active anti-inflammatory ingredients, and antioxidants (Hamzah et al., 2019). This is by the research of Hermayanti (2020) that in 100 grams of Moringa leaf powder, there are 28.2 iron and 17.3 vitamin C. Iron is needed for the formation of haemoglobin, while vitamin C can make the iron in Moringa leaves absorbed by the body. Maximum consumption. Kashyap et al., (2022) linked the consumption of Moringa leaves with weight gain and the results proved that Moringa leaves can prevent weight loss due to the excess protein content of the Moringa plant. The higher serum ferritin level with the duration of ferrous sulfate administration in this study is not the same as the physiological conditions during pregnancy.

By research conducted by Suparyanto (2023) which compared serum ferritin levels. His research found that serum ferritin levels reached the lowest levels in the second trimester compared to the first and third trimesters. However, serum ferritin levels in the first trimester are higher than in the third. Gao (2015) also stated that liver ferritin levels in pregnant rats increased early in pregnancy and peaked on the third day of pregnancy. 9, but then decreased drastically until the end of pregnancy.

Based on research by Gambling (2004) on rats stated that iron supplementation in pregnant rats had a more effective effect on increasing Hb and pregnancy outcomes when given starting on the seventh day of pregnancy, it was stated that the weight of children born was heaviest in the group given iron supplementation starting on the seventh day compared to those given from the first day and the 14th day of pregnancy and giving from the first day is better than giving from the 14th day of pregnancy. Based on research by Gambling (2004) can be used as the basis that the faster the administration of iron the faster the condition of maternal anemia will improve, ultimately affecting the resulting pregnancy outcomes. In this research.

These results are in line with a study conducted by Gambling (2004) which stated that pregnant rats that were given iron supplements from the start of pregnancy (day 0.5 of gestation) had higher levels of ferritin mRNA than rats that were given iron supplements from 7.5 and 12.5 pregnancies. When iron levels are low, ferritin synthesis will decrease. Conversely, when intracellular iron levels are high, ferritin synthesis will increase. However,

ferritin will still be synthesized under some conditions even though intracellular iron levels are high (Moreira et al., 2020).

Serum ferritin levels are related to iron stores in the body; therefore, serum ferritin is used as a reliable parameter to determine iron deficiency in the body (Dignass et al., 2018). Although serum ferritin is the best indicator of iron stores, it is not sensitive to body iron status in people with infection, inflammation or cancer. Apart from being influenced by intracellular iron levels, ferritin synthesis is also influenced by pro-inflammatory cytokines, such as TNFα (Tumor Necrosis Factor α), Interleukin1 (IL1) and Interleukin 6 (IL6) (Daru et al., 2017).

Serum ferritin levels higher with the duration of the tablet administration in this study were not the same as the physiological conditions that occur during pregnancy. Her research found that serum ferritin levels reached the lowest levels in the second trimester compared to the first and third trimesters. However, serum ferritin levels in the first trimester are higher than in the third trimester (Benson et al., 2021).

This study showed improved outcomes after administration of Fe Tablets and Moringa Leaf Capsules in the form of increased Hepcidin levels and increased Ferritin levels in the group of rats treated to resemble anemia, especially in treatment group 2 with the dose of Moringa Leaf Capsules 36 mg/kgBB. With further research, it can be considered that Fe Tablets and Moringa Leaf Capsules can prevent anemia in pregnancy.

The strength of this study is to examine 2 markers of anemia, namely hepcidin and ferritin and to treat anemic pregnant rats so that they can increase Hb levels in anemic pregnant rats, thereby reducing morbidity and mortality. For further researchers and for practitioners to be able to conduct clinical trials on this Moringa leaf extract so that it is safe for consumption by pregnant women.

CONCLUSIONS

The conclusions that can be obtained are the average hepcidin level in the Moringa leaf group (P2) was higher than the other two groups, namely 216.362 ± 29.90. The average ferritin level in the Moringa leaf group (P2) was higher than the other two groups, namely 2.308 ± 0.320. There was an effect on hepcidin levels after being given Fe tablets (P1) and Moringa leaf capsules (P2) to anemic pregnant rats and there was an effect on ferritin levels after being given Fe tablets (P1) and Moringa leaf capsules (P2) to anemic pregnant rats.

REFERENCE

Agustina, W. (2019). Perbandingan Kadar Hemoglobin Pada Ibu Hamil Yang Mengkomsumsi Tablet Besi Dengan Dan Tanpa Vitamin C di Wilayah Kerja Puskesmas Langsa Lama Tahun 2019. *Jurnal Nasional Ilmu Kesehatan*, *2*(2), 76–87. http://journal.unhas.ac.id/index.php/jnik/article/view/7080/4347

Arima, L. A. T., Murbawani, E. A., & Wijayanti, H. S. (2019). Hubungan Asupan Zat Besi Heme, Zat Besi Non-Heme Dan Fase Menstruasi Dengan Serum Feritin Remaja Putri. *Journal of Nutrition College*, *8*(2), 87. https://doi.org/10.14710/jnc.v8i2.23819

Benson, C. S., Shah, A., Frise, M. C., & Frise, C. J. (2021). Iron deficiency anaemia in pregnancy: A contemporary review. *Obstetric Medicine*, *14*(2), 67–76. https://doi.org/10.1177/1753495X20932426

BPS. (2019). *Statistik Indonesia 2019*. https://www.bps.go.id/publication/2019/07/04/statistik-indonesia-2019.html

Daru, J., Colman, K., Stanworth, S. J., De La Salle, B., Wood, E. M., & Pasricha, S. R. (2017). Serum ferritin as an indicator of iron status: What do we need to know? *American Journal of Clinical Nutrition*, *106*, 1634S-1639S. https://doi.org/10.3945/ajcn.117.155960

Diana, S. (2017). *Perbedaan Kadar Hepsidin dan Ferritin Antara Ibu Hamil yang Anemia dan Tidak Anemia*.

Dignass, A., Farrag, K., & Stein, J. (2018). Limitations of Serum Ferritin in Diagnosing Iron Deficiency in Inflammatory Conditions. *International Journal of Chronic Diseases*, *9394060*, 1–11. https://doi.org/10.1155/2018/9394060

Gambling, L., Andersen, H. S., Czopek, A., Wojciak, R., Krejpcio, Z., & McArdle, H. J. (2004). Effect of timing of iron supplementation on maternal and neonatal growth and iron status of iron-deficient pregnant rats. *Journal of Physiology*, *561*(1), 195–203. https://doi.org/10.1113/jphysiol.2004.068825

Gao, G., Liu, S. Y., Wang, H. J., Zhang, T. W., Yu, P., Duan, X. L., Zhao, S. E., & Chang, Y. Z. (2015). Effects of pregnancy and lactation on iron metabolism in rats. *BioMed Research International*, *105325*, 1–9. https://doi.org/10.1155/2015/105325

Gumilang, L., Judistiani, T. D., Nirmala, S. A., & Wibowo, A. (2021). Korelasi Asupan Zat Besi dan Protein dengan Kadar Ferritin Serum Ibu Hamil di Kabupaten Waled dan Sukabumi. *Higeia*, *5*(2), 231–241.

Hamzah, H., & Yusuf, N. R. (2019). Analisis Kandungan Zat besi (Fe) Pada Daun Kelor (Moringa oleifera Lam.) Yang Tumbuh dengan Ketinggian Berbeda di Daerah Kota Baubau. *Indo. J. Chem. Res.*, *6*(2), 88–93. https://doi.org/10.30598//ijcr.2019.6-has

Hermayanti, D., Setiawan, W., & Azhar, R. M. (2020). The Effect of Moringa Leaf (Moringa oleifera Lam) and Vitamin C Combination Extract in Improving Anemia Indicators Deficiency of White Rice Iron Male Diet Low Rice Iron. *Jurnal Saintika Medika*, *16*(2), 104–114.

Jayanti, Y. D. (2018). Pengaruh Waktu Pemberian Suplemen Ferro Sulfat Terhadap Kadar Serum Ferritinpada Tikus Putih (Rattus Norvegicus) Bunting. *Jurnal Kebidanan*, *7*(2), 106–111. https://doi.org/10.35890/jkdh.v7i2.102

Kashyap, P., Kumar, S., Riar, C. S., Jindal, N., Baniwal, P., Guiné, R. P. F., Correia, P. M. R., Mehra, R., & Kumar, H. (2022). Recent Advances in Drumstick (Moringa oleifera) Leaves Bioactive Compounds: Composition, Health Benefits, Bioaccessibility, and Dietary Applications. *Antioxidants*, *11*(2), 1–37. https://doi.org/10.3390/antiox11020404

Kemenkes RI. (2018). *Laporan Nasional Riskesdas 2018*. Jakarta : Kementerian Kesehatan RI.

Krisnanda, R. (2020). Vitamin C membantu dalam absorpsi zat besi pada anemia defisiensi besi. *Jurnal Penelitian Perawat Profesional*, *2*(3), 279–286.

Kurniasih. (2013). *Khasiat dan manfaat daun kelor untuk penyembuhan berbagai penyakit*.

Yogyakarta : Pustaka Baru Press.

Kurniati, I. (2020). Anemia Defisiensi Zat Besi (Fe). *Jurnal Kedokteran Universitas Lampung*, *4*(1), 18–33.

Mani, L., Fatimah-Muis, S., & Kartini, A. (2020). Korelasi kadar hepcidin dan asupan makanan dengan serum transferrin reseptor dan hemoglobin pada remaja stunted overweight. *Jurnal Gizi Indonesia*, *8*(1), 51–59. https://doi.org/10.14710/jgi.8.1.51-59

Millah, A. S. (2019). Hubungan Konsumsi Tablet Fe Dengan Kejadian Anemia Pada Ibu Hamil Di Desa Baregbeg Wilayah Kerja Puskesmas Baregbeg Kabupaten Ciamis Tahun 2018. *Jurnal Keperawatan Galuh*, *1*(1), 12. https://doi.org/10.25157/jkg.v1i1.1787

Moreira, A. C., Mesquita, G., & Gomes, M. S. (2020). Ferritin: An inflammatory player keeping iron at the core of pathogen-host interactions. *Microorganisms*, *8*(4), 1–20. https://doi.org/10.3390/microorganisms8040589

Pane, M. H., Rahman, A. O., & Ayudia, E. I. (2021). Gambaran Penggunaan Obat Herbal Pada Masyarakat Indonesia Dan Interaksinya Terhadap Obat Konvensional Tahun 2020. *Journal of Medical Studies*, *1*(1), 40–62. https://online-journal.unja.ac.id/joms/article/view/14527

Saito, H. (2014). Metabolism of iron stores. *Nagoya Journal of Medical Science*, *76*(3–4), 235–254.

Sumailan, G. P., Dinengsih, S., & Siauta, J. (2021). The Analysis of Efforts to Prevent Anemia in Pregnant Women during the Covid 19 Pandemic. *Jurnal Kebidanan Midwiferia*, *7*(2), 66–76. https://doi.org/10.21070/midwiferia.v7i2.1631

Suparyanto, T., Anggraeni, M., & Yolandia, R. A. (2023). Hubungan Pemberian Tablet Zik, Gaya Hidup, dan Asupan Protein Terhadap Kadar Feritin Pada Ibu Hamil Trisemester III di Rumah Sakit Krakatau Medika Cilegon Tahun 2022. *SENTRI: Jurnal Riset Ilmiah*, *2*(4), 978–993. https://doi.org/10.55681/sentri.v2i4.695

Turawa, E., Awotiwon, O., Dhansay, M. A., Cois, A., Labadarios, D., Bradshaw, D., & Wyk, V. P. Van. (2021). Prevalence of anaemia, iron deficiency, and iron deficiency anaemia in women of reproductive age and children under 5 years of age in south africa (1997–2021): A systematic review. *International Journal of Environmental Research and Public Health*, *18*(23), 2–17. https://doi.org/10.3390/ijerph182312799

Wahyuni, E. S. (2021). Pengaruh Suplementasi Fe dan Vitamin C terhadap Hemoglobin dan Indeks Eritrosit Remaja Putri. *Jurnal Kesehatan*, *12*(2), 162.

WHO. (2017). *Nutritional Anaemias : Tools For Effective Prevention and Control*. Ganeva : World Health Organization. https://www.who.int/publications/i/item/9789241513067

Young, I., Parker, H. M., Rangan, A., Prvan, T., Cook, R. L., Donges, C. E., Steinbeck, K. S., O'Dwyer, N. J., Cheng, H. L., Franklin, J. L., & O'Connor, H. T. (2018). Association between haem and non-haem iron intake and serum Ferritin in healthy young women. *Nutrients*, *10*(1), 1–13. https://doi.org/10.3390/nu10010081